Version f Amended Specificati n Paragraphs With Markings t Show Changes Made:

NOTE: Deletions are marked by brackets and bold text.

Paragraph 1:

Transporters are generally classified by structure and the type of mode of action. In addition, transporters are sometimes classified by the molecule type that is transported, for example, sugar transporters, chlorine channels, potassium channels, etc. There may be many classes of channels for transporting a single type of molecule (a detailed review of channel types can be found at Alexander, S.P.H. and J.A. Peters: Receptor and transporter nomenclature supplement. Trends Pharmacol. Sci., Elsevier, pp. 65-68 (1997) **[and http://www-biology.ucsd.edu/~msaier/transport/titlepage2.html]**.

Paragraph 2:

Ion channels are generally classified by structure and the type of mode of action. For example, extracellular ligand gated channels (ELGs) are comprised of five polypeptide subunits, with each subunit having 4 membrane spanning domains, and are activated by the binding of an extracellular ligand to the channel. In addition, channels are sometimes classified by the ion type that is transported, for example, chlorine channels, potassium channels, etc. There may be many classes of channels for transporting a single type of ion (a detailed review of channel types can be found at Alexander, S.P.H. and J.A. Peters (1997). Receptor and ion channel nomenclature supplement. Trends Pharmacol. Sci., Elsevier, pp. 65-68 **[and http://www-biology.ucsd.edu/~msaier/transport/toc.html]**.

Paragraph 3:

The comparison of sequences and determination of percent identity and similarity between two sequences can be accomplished using a mathematical algorithm. (*Computational Molecular Biology*, Lesk, A.M., ed., Oxford University Press, New York, 1988; *Biocomputing: Informatics and Genome Projects*, Smith, D.W., ed., Academic Press, New York, 1993; *Computer Analysis of Sequence Data, Part 1*, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, 1994; *Sequence Analysis in Molecular Biology*, von Heinje, G., Academic Press, 1987; and

Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991). In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (*J. Mol. Biol.* (48):444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package **[(available at http://www.gcg.com)]**, using either a Blossom 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (Devereux, J., *et al., Nucleic Acids Res. 12(1)*:387 (1984)) **[(available at http://www.gcg.com)]**, using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. In another embodiment, the percent identity between two amino acid or nucleotide sequences is determined using the algorithm of E. Myers and W. Miller (CABIOS, 4:11-17 (1989)) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

Version of Amended Claims With Markings to Show Changes Made:

24. (Amended) A process for producing a polypeptide comprising SEQ ID NO:2, the process comprising culturing the host cell of claim 9 under conditions sufficient for the production of said polypeptide, and recovering said polypeptide from the host cell culture, wherein said isolated nucleic acid molecule encodes a polypeptide comprising SEQ ID NO:2.

28. (Amended) A vector according to claim 8, wherein said isolated nucleic acid molecule encodes a polypeptide comprising SEQ ID NO:2 and is inserted into said vector in proper orientation and correct reading frame such that a polypeptide comprising [the protein of] SEQ ID NO:2 may be expressed by a cell transformed with said vector.

REMARKS

Applicants have studied the Office Action mailed May 1, 2002. It is respectfully submitted that the application is in condition for allowance. Reconsideration and allowance of the pending claims in view of the above amendments and the following remarks is respectfully requested.

Drawings:

The Examiner states that the instant specification does not comply with 37 C.F.R. § 1.84(U)(1) because drawings contained on multiple sheets, which are intended to form one complete view, must be identified by the same number followed by a capital letter.

In response, Applicants intend to submit new formal drawings, having correct numbering of drawing sheets, upon allowance of the presently rejected claims.

Sequence Identifiers:

The Examiner states that drawings in the instant specification do not comply with 37 C.F.R. § 1.821(d) because a sequence identifier is required for sequences presented in the drawings.

In response, Applicants intend to submit new formal drawings, having SEQ ID NOs appropriately inserted, upon allowance of the presently rejected claims. Presently, SEQ ID NOs are referenced in the "Description of the Figure Sheets" section on page 15 of the specification.

Hyperlinks:

The Examiner objected to the disclosure as containing embedded hyperlinks and/or other browser-executable code.

In response, Applicants have deleted all hyperlinks from the specification, as indicated above by the replacement paragraphs.

Listing of references:

The Examiner stated that the listing of references in the specification is not a proper information disclosure statement. The Examiner states that, unless the references have been cited on form PTO-892, they have not been considered.

In response, Applicants acknowledge that the references listed in the specification are incorporated by reference pursuant to MPEP §608.01(p) and, to be considered by the Examiner, references must be cited as a proper information disclosure statement on form PTO-892.

Other objection to the specification:

The Examiner objected to the specification because the text in line 18 on page 16, and lines 5 and 21 on page 27, refers to "[e]xperimental data as provided in Figure 1", and the Examiner states that Figure 1 of the instant application presents no experimental data.

In response, Applicants respectfully assert that Figure 1 does present experimental data. Specifically, Figure 1 provides the nucleotide sequence of a transcript sequence that was sequenced and annotated and verified by cDNA cloning and isolation (page 1 of Figure 1); the results of BLAST sequence similarity analysis and virtual Northern blot analysis against dbEST (page 2 of Figure 1); and tissue expression information (page 2 of Figure 1). Any of this information can be considered experimental data.

Rejection of claims 4, 8-9, and 24-29 under 35 USC §101 and §112, 1st paragraph:

The Examiner has rejected claims 4, 8-9, and 24-29 under 35 U.S.C.§101 and §112, 1st paragraph. In summary, the Examiner has stated that these claims are drawn to an invention with no apparent or disclosed specific and substantial credible utility. The Examiner states that the instant application does not disclose a specific biological role for the disclosed protein or its significance to a particular disease, disorder or physiological process which one would wish to manipulate for a desired clinical effect.

In making these rejections, the Examiner states that the instant claims are drawn to isolated nucleic acid molecules encoding a protein of as yet undetermined function or biological significance. The Examiner states that until some actual and specific significance can be attributed to the protein encoded by the claimed nucleic acid, or the gene encoding it, the instant invention is incomplete. The Examiner states that, in the absence of knowledge of the natural

ligands or biological significance of the disclosed protein, there is no immediately obvious patentable use for it. The Examiner states that, to employ a protein of the instant invention in the identification of substances that inhibit or induce its activity is clearly to use it as the object of further research, which has been determined by the courts to be a utility that, alone, does not support patentability.

Applicants respectfully traverse these rejections based on the following remarks.

Contrary to the Examiner's assertions, the claimed isolated nucleic acid molecules, such as SEQ ID NOS:1 and 3, that encode a specified amino acid sequence, SEQ ID NO:2, and methods of making and using such nucleic acid molecules have several uses that meet the requirements of 35 U.S.C.§101 and the first paragraph of 35 U.S.C.§112. These, as well as the accepted state of the art view that such molecules have uses within the commercial marketplace in the drug development cycle, since they encode previously unidentified members of important pharmaceutical targets, establishes the utility of the claimed invention.

The utility requirement of a claimed invention requires that an invention must have a specific, substantial and credible utility. These requirements are defined in broad terms in cases such as *Brenner v. Manson,* 148 USPQ 689 (S. Ct. 1966) and the recently adopted Utility Guidelines from the USPTO.

However, the notion that a recognized valuable addition to even entry points of the drug discovery cycle advances the art sufficient to establish a "usefulness" of a claimed invention should not be ignored. This is supported by previous case law (e.g., *Nelson v. Bowler*, 206 USPQ 881 (CCPA 1980)). Accordingly, the present invention, which is drawn to isolated nucleic acid molecules that encode a novel transporter protein, specifically an anion transporter (SEQ ID NO:2), has valuable commercial utilities in the drug discovery process by providing previously unidentified members of an important pharmaceutical target class. The present invention provides sufficient knowledge and information that is beneficial to the public, and provides sufficient guidance for researchers to use the claimed subject matter to develop disease treatments and/or diagnostics. It is well recognized that transporter proteins are among the most important target for drug action (see, e.g., pages 1-14 of the specification). The public disclosure of a new member of the transporter family through the patenting process clearly advances the art and augments the capabilities of biomedical researchers to combat illnesses.

The utility rejection raised by the Examiner also conflicts with the case *Juicy Whip v. Orange Bang* (Fed. Cir. 1999). *Juicy Whip* held that, in order to violate the utility requirement, an invention must be "totally incapable of achieving a useful result." The polypeptides and encoding nucleic acid molecules of the present invention are well known in the art to be valuable drug targets and therefore have readily apparent commercial utilities, such as for screening potential drug compounds, producing antibodies, developing hybridization probes and primers, etc. In addition to the uses disclosed in the specification and discussed herein for the polynucleotides of the present invention, other utilities are readily apparent to one of ordinary skill in the art based on the observed tissue specific expression patterns. Specifically, the nucleic acid molecules of the present invention are expressed in human fetal lung, and virtual Northern blot analysis further indicates expression in the head/neck region (as indicated in Figure 1). Thus, for example, the proteins/nucleic acids of the present invention are commercially useful for developing therapeutic agents for treating pathologies affecting these tissues, or for use as tissue markers. Therefore, the present invention is not "totally incapable of achieving a useful result." Instead, it is useful.

Contrary to the Examiner's assertions, Applicants have provided sufficient guidance such that undue experimentation would not be required by one of ordinary skill in the art to determine which biological activities the disclosed polypeptides are involved in so as to know how to use the claimed invention. For example, Applicants have characterized the transporter protein of SEQ ID NO:2 as an anion transporter protein with substantial similarity to those that transport sulfate anions, thereby further enabling one of ordinary skill in the art to use the claimed invention. Given the guidance provided in the specification and figures in combination with the knowledge in the art regarding the known biological roles of known anion transporters, one of ordinary skill in the art would know how to use the novel transporter proteins, and encoding nucleic acid molecules, provided by Applicants without undue experimentation.

The function of anion transporters, in contrast to transporters in general, is well known in the art and is specifically described on pages 5-6 of the specification. As indicated on pages 5-6, anion transporters, such as sulfate transporters, have been implicated in diseases such as Pendred syndrome. SLC26A5 transporter protein (also known as prestin), which is an anion transporter that shares a high degree of similarity with the novel transporter of the present invention, may act as a motor protein in cochlear outer hair cells. Anion transporters complement cation transporters,

and enable cells to maintain a surplus of anions in the cytoplasm, thereby giving the interior of the cell a negative charge relative to the exterior environment and generating the voltage difference characteristic of living cells. Such functions are quite specific for anion transporters and differentiate them from other proteins, including other transporter proteins. As such, these functions are clearly specific enough to define uses for novel anion transporters, and encoding nucleic acid molecules, in the drug discovery process, and to enable one of ordinary skill in the art to use the claimed invention without undue experimentation.

Because of the essential roles that anion transporters play in such important physiological processes as anion transport across plasma membranes and maintenance of the voltage differential between cells and the extracellular environment, it is clear that the disclosure of novel anion transporters satisfies a need in the art by providing important new compositions that are useful towards the prevention, diagnosis, and treatment of numerous human disorders. For example, as indicated on page 6 of the specification, genes encoding anion transporters have been implicated in a number of diseases, including Pendred syndrome, diastrophic dysplasia, and congenital chloride diarrhea. Pendred syndrome is an autosomal recessive disease characterized by goiter and congenital sensorineural deafness. Pendred syndrome may afflict as many as 7.5-10 out of every 100,000 individuals and account for 10% of all cases of hereditary deafness. Consequently, one of ordinary skill in the art would recognize that novel anion transporters, and encoding nucleic acid molecules, have valuable medical and commercial utilities.

Thus, there is overwhelming evidence in the art to support the utility of novel transporter proteins and encoding nucleic acid molecules. Not all nucleic acid molecules, and actually a very limited number, of the 3 billion bases that make up the human genome will encode a protein for these and the other disclosed uses. These uses are quite specific for the transporter family of proteins, particularly anion transporters, and each is a specific composition of matter having substantial, specific and credible uses that the vast majority of other isolated nucleic acid molecules do not possess.

By placing a new member of the transporter protein family into the public domain through the patenting process, the present invention is not only a clear advancement over the prior art (a newly discovered protein/gene) but also enables significant advancement in medicine and further discovery. The Utility requirement cannot be used to contradict the reasons for the patent system, i.e., to encourage early disclosures of inventions so that others can benefit from, improve upon,

and further develop such inventions. This is particularly important in medicine, wherein early disclosure of key inventions (such as new transporter proteins and encoding nucleic acid molecules) is needed to facilitate the early development of new therapies and diagnostics to treat illnesses.

The grant of a patent to the claimed isolated nucleic acid molecule and the resultant disclosure of the nucleic acid and protein sequences to the public will certainly shorten the process for medical researchers to discover other novel uses for the present transporter-encoding nucleic acids. One example disclosed in the specification is that the present nucleic acid molecules can be used to produce protein targets for identifying agents that bind to the protein targets and modulate protein function. Such agents that bind to a protein target and modulate cellular processes such as ion transport or cell signaling may subsequently be developed and refined for use in mammalian therapeutic applications. All of this later discovery and refinement will be done using the presently claimed material. These uses are clearly commercial and substantial uses that are specific for a very limited number of proteins/nucleic acid molecules.

In addition to serving as targets for developing molecular probes and therapeutic agents, the disclosed uses of the claimed nucleic acid molecules as probes, primers, and chemical intermediates, particularly in biological assays, is sufficient to satisfy the requirements of 35 USC §101 and §112. The claimed invention is directed to nucleic acid sequences, such as SEQ ID NOS:1 and 3, that encode a transporter protein with a specified amino acid sequence (SEQ ID NO:2). Exemplary uses of the nucleic acid sequences are clearly recited in the specification on, for example, pages 42-61. Among the examples, the nucleic acid molecules are useful as hybridization probes for messenger RNA molecules, transcript/cDNA molecules, genomic DNA, and variants thereof. An expression vector comprising the nucleic acid sequences can be made that expresses the transporter protein. Such uses are specific for the claimed nucleic acid molecules, and the products of such uses will be clearly different (and hence specific for the claimed molecules) than what would be produced using a different nucleic acid molecule for the same purpose.

In view of law and fact, the utility standard interpreted by the USPTO guidelines is too high. The commercial value of previously unidentified members of the transporter protein family, members of which are well known in the art to be commercially valuable drug targets, should be

sufficient to satisfy the utility requirement. Therefore, applicants respectfully request that the Examiner withdraw the rejections.

Rejection of claims 24, 28, and 29 under 35 USC §112, 2nd paragraph:

The Examiner rejected claim 24 as being vague and indefinite because the identity of the polypeptide being produced is not indicated (because thousands of different polypeptides can be produced by culturing a host cell). The Examiner also rejected claims 24, 28, and 29 as being incomplete because they are not limited to an isolated nucleic acid molecule encoding a polypeptide due to their ultimate dependence on part (d) of claim 4.

In response, Applicants have amended claim 24 to clarify that the polypeptide that is intended to be produced is a polypeptide comprising SEQ ID NO:2, and to clarify that the claimed process is intended to be limited to a process that employs a nucleic acid molecule that encodes a polypeptide. Additionally, Applicants have amended claim 28 to clarify that the claimed vector contains a nucleic acid molecule that encodes a polypeptide. Claim 29 is dependent on claim 28 and therefore clarified by way of the amendment to claim 28.

Thus, in view of these amendments and remarks, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 24, 28, and 29 under 35 USC §112, 2nd paragraph.

Conclusions

Claims 4, 8-9, and 24-29 are currently pending. Claims 24 and 28 have been amended, as indicated above.

The amendments to the specification and claims add no new subject matter and their entry is respectfully requested.

In view of the above remarks and amendments, Applicants respectfully submit that the application and claims are in condition for allowance, and request that the Examiner reconsider and withdraw the objections and rejections. If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is invited to call the undersigned agent at (240) 453-3812 should the Examiner believe a telephone interview would advance prosecution of the application.

Respectfully submitted,
CELERA GENOMICS

By: _____
Justin D. Karjala, Reg No. 43,704

Date: September 3, 2002

Celera Genomics Corporation
45 West Gude Drive, C2-4#20
Rockville, MD 20850
Tel: 240-453-3812
Fax: 240-453-3084